PTO/SB/08a (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

	Application Number		10590054	
INFORMATION BIOGLOGUES	Filing Date		2006-08-21	
INFORMATION DISCLOSURE	First Named Inventor	Jacob	WESTMAN et al	
STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Art Unit		1645	
(Notion Submission under or of it 1.00)	Examiner Name			
	Attorney Docket Number		WESTMAN=3	

U.S.PATENTS Remove											
					0.3.1	AILNIS		<u> </u>		l	
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue D)ate	Name of Pate of cited Docu	entee or Applicant ment	Releva		Lines where ges or Relev	
	1										
If you wis	h to ac	dd additional U.S. Pater	nt citatio	n inform	ation pl	ease click the	Add button.		Add		
			U.S.P.	ATENT	APPLIC	CATION PUBI	LICATIONS		Remove		
Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publica Date	ition	Name of Pate of cited Docu	entee or Applicant ment	Releva		Lines where ges or Relev	
	1										
If you wis	h to ac	dd additional U.S. Publis	shed Ap	plication	citation	n information p	please click the Add	d button	Add		
				FOREIG	SN PAT	ENT DOCUM	ENTS		Remove		
Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²		Kind Code ⁴	Publication Date	Name of Patentee Applicant of cited Document	or -	vhere Rel	or Relevant	T5
	1										
If you wish to add additional Foreign Patent Document citation information please click the Add button Add											
NON-PATENT LITERATURE DOCUMENTS Remove											
Examiner Initials* Cite No Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.								T 5			

Application Number		10590054
Filing Date		2006-08-21
First Named Inventor Jacob		WESTMAN et al
Art Unit		1645
Examiner Name		
Attorney Docket Number		WESTMAN=3

1	Abstracts of Papers Part 2, 226th ACS National Meeting, American Chemical Society, New York, NY, September 7-11, 2003.	
2	NAHI, H. et al, "Effects of PRIMA-1 on Chronic Lymphocytic Leukemia cells with and without hemizygous p53 deletion", British Journal of Haematology, vol. 127, 2004, pp. 285-291.	
3	NIELSEN, Arnold T., "Systems with Bridgehead Nitrogen. beta-Ketols of the 1-Azabicyclo[2.2.2]octane Series", Journal of Organic Chemistry, vol. 31, April 1966, pp. 1053-1059.	
4	OKUDA, Yoshinobu et al., "Regulatory role of p53 in experimental autoimmune encephalomyelitis", Journal of Neuroimmunology, vol. 135, 2003, pp. 29-37.	
5	REHMAN, Abdur et al., "Proteomic identification of heat shock protein 90 as a candidate target for p53 mutation reactivation by PRIMA-1 in breast cancer cells", Breast Cancer Research, vol. 7, No. 5, 2005, pp. R765-R774.	
6	SAKAMURI, Sukumar et al., "Synthesis of 2-alkyl-3-aryl-substituted quinuclidines as novel dopamine transporter inhibitors", Tetrahedron Letters, vol. 41, 2000, pp. 9949-9952.	
7	SCHIEWECK, Frank et al., "Synthesis of geminal bis(hydroxymethyl)pyrrolidine and pyrrolizidine imino sugars", J. Chem. Soc., Perkin Trans. 1, 2001, pp. 3409-3414.	
8	SEKHAR, Konjeti et al., "NADPH Oxidase Activity Is Essential for Keap1/Nrf2-mediated Induction of GCLC in Response to 2-Indol-3-yl-methylenequinuclidin-3-ols", Cancer Research, vol. 63, September 1, 2003, pp. 5636-5645.	
9	SHERR, Charles J., "Tumor surveillance via the ARF-p53 pathway", Genes & Dev., vol. 12, 1998, pp. 2984-2991.	
10	SINGH, Tara et al., "Antimalarials. Some Quinuclidine Derivatives of 7-Chloro-4-aminoquinoline and 6-Methoxy-8-aminoquinoline", Research Laboratories of Aldrich Chemical Company, Vol. 12, May 1969, pp. 524-526.	
11	SYMONDS, Holly et al., "p53-Dependent Apoptosis Suppresses Tumor Growth and Progression In Vivo", Cell, Vol. 78, August 26, 1994, pp.703-711.	

Application Number		10590054
Filing Date		2006-08-21
First Named Inventor	Jacob	WESTMAN et al
Art Unit		1645
Examiner Name		
Attorney Docket Number		WESTMAN=3

12	TONDER, Janne E., "Exploring the Stereoselectivity in the Peterson Reaction of Several 2-Substituted 1-Azabicyclo [2.2.2]octan-3-ones", Tetrahedron, vol. 56., 2000, pp. 1139-1146.	
13	VOROB'EVA, et al., "Reaction of 2-Methylene-3-Oxoquinuclidine with Nucleophilic Reagents", Chemistry of Heterocyclic Compounds, vol. 10, 1977, pp. 1098-1104.	
14	YANINA, A.D., et al., "Synthesis and pharmacological properties of 2- and 2,3-substituted quinuclidines", 1-Pharmacology, vol. 108, 1988, p. 71.	
15	BARDEESY, Nabeel et al., "Clonal Expansion and Attenuated Apoptosis in Wilms' Tumors Ate Associated with p53 Gene Mutations", Cancer Research, vol. 55, January 15, 1995, pp. 215-219.	
16	BENNETT, Martin et al., "Cell Surface Trafficking of Fas: A Rapid Mechanism of p53-Mediated Apoptosis", Science, vol. 282, October 9, 1998, pp. 290-293.	
17	BEROUD et al, "p53 gene mutation: software and database", Nucleic Acids Research, Vol. 26, No. 1, 1998, pp. 200-204.	
18	BONAFE et al., "The different apoptotic potential of the p53 codon 72 alleles increases with age and modulates in vivo ischaemia-induced cell death", Cell Death and Differentiation, vol. 11, 2004, pp. 962-973.	
19	BONDARENKO et al., "Synthesis and antirrhythmic activity of derivatives of 3-aminoquinuclidine and 2-(aminomethyl) Quinuclidine", Pharmaceutical Chemistry Journal, vol. 12., 1978, pp. 1452-1455.	
20	BYKOV et al., "Mutant p53-dependent growth suppression distinguishes PRIMA-1 from known anticancer drugs: a statistical analysis of information in the National Cancer Institute database", Carcinogenesis, vol. 23, No. 12, 2002, pp.2011-2018.	
21	BYKOV et al., "Novel cancer therapy by reactivation of the p53 apoptosis pathway", Annals of Medicine, vol. 35, 2003, pp. 458-465.	
22	BYKOV et al., "PRIMA-1MET synergizes with cisplatin to induce tumor cell apoptosis", Oncogene, 2005, pp. 1-8.	

Application Number		10590054
Filing Date		2006-08-21
First Named Inventor	Jacob	WESTMAN et al
Art Unit		1645
Examiner Name		
Attorney Docket Number		WESTMAN=3

23	BYKOV, et al., "Reactivation of Mutant p53 and Induction of Apoptosis in Human Tumor Cells by Maleimide Analogs", The Journal of Biological Chemistry, vol. 280, No. 34, August 26, 2005, pp. 30384-30391.	
24	BYKOV et al., "Restoration of the tumor suppressor function to mutant p53 by a low-molecular-weight compound", Nature Medicine, vol. 8, no. 3, March 2002, pp. 282-288.	
25	BYKOV et al., "Small molecules that reactivate mutant p53", European Journal of Cancer, vol. 39, 2003, pp. 1828-1834.	
26	CHAKRABARTI et al., "Rearrangement of 2-[1(3H)-Oxodihydrobenzo[c]FURAN-3-YL] Quinuclidin-3-Ones to Tetrahydrobenzo[b]Quinolizines. A novel Synthesis of Benzo[b]Quinolizine Ring Systems", Tetrahedron Letters, Vol. 26, No. 35, 1985, pp. 4245-4246.	
27	CHIPUK et al., "Pharmacologic activation of p53 elicits Bax-dependent apoptosis in the absence of transcription", Cancer Cell, vol. 4, November 2003, pp. 371-381.	
28	EVAN et al., "A Matter of Life and Cell Death", Science, vol. 281, August 28, 1998, pp. 1317-1322.	
29	FISHER et al., "The Fused Quinuclidine-valerolactone system", Tetrahedron, vol. 31, 1975, pp. 317-325.	
30	GOTTLIEB et al., "p53 and Apoptosis", Cancer Biology, Vol. 8, 1998, pp. 359-368.	
31	KO et al., "p53: puzzle and paradigm", Genes & Development, vol. 10, 1996, pp. 1054-1072.	
32	KUMAR et al., "Clay Catalyzed Highly Selective O-Alkylation of Primary Alcohols with Orthoesters", Tetrahedron Letters, Vol. 38, No. 20, 1997, pp. 3619-3622.	
33	LANGER et al., "New Methods of Drug Delivery", SCIENCE, vol. 249, No. 4976, September 28, 1990, pp. 1527-1533.	

Application Number		10590054
Filing Date		2006-08-21
First Named Inventor Jacob		WESTMAN et al
Art Unit		1645
Examiner Name		
Attorney Docket Number		WESTMAN=3

	34	LEE et al., "Expression proteomics to p53 mutation reactivation with PRIMA-1 in breast cancer cells", Biochemical and Biophysical Research Communications, vol. 349, 2006, pp. 1117-1124.						
	35	LI et al., "Selective induction of apoptosis in mutant p53 premalignant and malignant cancer cells by PRIMA-1 through the c-Jun-NH2-kinase pathway", Mol Cancer Ther, vol. 4, no.6, June 2005, pp. 901-909.						
	36	LIANG et al., "Functional p53 blocks progestin-induced VEGF expression in human breast cancer cells", Dalton cardiovascular Research Center and the Dept. of Biomedical Sciences, University of Missouri, Columbia, MO,						
	37	LOWE, III et al., "2-Aryl-azabicyclo[2.2.2]octanes as Novel Nonpeptide Substance P Antagonists", Bioorganic & Medicinal Chemistry Letters, vol. 4, no. 6, 1994, pp. 839-842.						
	38	LOWE et al., "p53 Status and the Efficacy of Cancer Therapy in Vivo", Science, New Series, Vol. 266, No. 5186, November 4, 1994, pp. 807-810.						
	39	MYERS et al., "A New Family of Small Molecules to Probe the Reactivation of Mutant p53", J. Am. Chem. Soc., July 15, 2004.						
	MORGAN et al., "Synthesis and Cardiac Electrophysiological Activity of 2- and 3-[(Substituted phenyl)alkyl] quinuclidines. Structure-Activity Relationships", J. Med. Chem., Vol. 30, 1987, pp. 2259-2269.							
	41	MOUNTZ et al., "Defective clonal deletion and anergy induction in TCR transgenic lpr/lpr mice", Immunology, Vol. 6, 1994, pp. 27-37.						
If you wis	h to a	dd additional non-patent literature document citation information please click the Add button Add						
EXAMINER SIGNATURE								
Examiner	Examiner Signature Date Considered							
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.								
Standard ST	¹ See Kind Codes of USPTO Patent Documents at <u>www.USPTO.GOV</u> or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.							

(Not for submission under 37 CFR 1.99)

Application Number		10590054
Filing Date		2006-08-21
First Named Inventor Jacob		WESTMAN et al
Art Unit		1645
Examiner Name		
Attorney Docket Number		WESTMAN=3

Plea	Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):						
	That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).						
OF	1						
	foreign patent o after making rea any individual d	information contained in the information of ffice in a counterpart foreign application, a isonable inquiry, no item of information con- esignated in 37 CFR 1.56(c) more than the 37 CFR 1.97(e)(2).	nd, to the knowledge of thatiance in the information d	ne person signing the certification isclosure statement was known to			
	See attached ce	rtification statement.					
	Fee set forth in 3	37 CFR 1.17 (p) has been submitted herewit	th.				
×	None						
	:	SIGNA		19 Diagram and CED 1 4/d) for the			
	A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.						
Sigi	nature	/jmf/	Date (YYYY-MM-DD)	2007-05-25			
Nar	Name/Print Jay M. Finkelstein F		Registration Number	21,082			
pub	This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed						

application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria**,

CERTIFICATION STATEMENT

VA 22313-1450.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

- 1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.
- A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a
 court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement
 negotiations.
- 3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
- 4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
- 5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
- 6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
- 7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
- 8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
 - 9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.